Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1644pnh

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	4	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	5	MAR 02	GBFULL: New full-text patent database on STN
NEWS	6	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	8	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	9	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	10	MAR 22	PATDPASPC - New patent database available
NEWS	11	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	12	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	13	APR 04	EMBASE - Database reloaded and enhanced
NEWS	14	APR 18	New CAS Information Use Policies available online
NEWS	15	APR 25	Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS	16	APR 28	Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus
NEWS	17	MAY 23	GBFULL enhanced with patent drawing images
NEWS	18	MAY 23	REGISTRY has been enhanced with source information from CHEMCATS
NEWS	19	JUN 06	The Analysis Edition of STN Express with Discover! (Version 8.0 for Windows) now available
NEWS	20	JUN 13	RUSSIAPAT: New full-text patent database on STN
NEWS	21	JUN 13	FRFULL enhanced with patent drawing images
NEWS	22	JUN 27	MARPAT displays enhanced with expanded G-group definitions and text labels
NEWS	23	JUL 01	MEDICONF removed from STN
NEWS	24	JUL 07	STN Patent Forums to be held in July 2005
NEWS	25	JUL 13	SCISEARCH reloaded
NEWS	26	JUL 20	Powerful new interactive analysis and visualization software, STN AnaVist, now available
NEWS	27	AUG 11	Derwent World Patents Index(R) web-based training during August
NEWS	28	AUG 11	STN AnaVist workshops to be held in North America
NEWS	29	AUG 30	CA/CAplus -Increased access to 19th century research documents
NEWS	30	AUG 30	CASREACT - Enhanced with displayable reaction conditions

NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items

```
 NEWS PHONE    Direct Dial and Telecommunication Network Access to STN
 NEWS WWW      CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that
specific topic.

  All use of STN is subject to the provisions of the STN Customer
  agreement.  Please note that this agreement limits use to scientific
  research.  Use for software development or design or implementation
  of commercial gateways or other similar uses is prohibited and may
  result in loss of user privileges and other penalties.

  * * * * * * * * * * * * * * STN  Columbus  * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:52:18 ON 02 SEP 2005

=> file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                     0.21       0.21

FILE 'MEDLINE' ENTERED AT 15:52:30 ON 02 SEP 2005

FILE 'EMBASE' ENTERED AT 15:52:30 ON 02 SEP 2005
COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.

FILE 'BIOSIS' ENTERED AT 15:52:30 ON 02 SEP 2005
Copyright (c) 2005 The Thomson Corporation

FILE 'SCISEARCH' ENTERED AT 15:52:30 ON 02 SEP 2005
Copyright (c) 2005 The Thomson Corporation

FILE 'CAPLUS' ENTERED AT 15:52:30 ON 02 SEP 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

=> s modified allergen
L1          464 MODIFIED ALLERGEN

=> s l1 and food allergen
L2           19 L1 AND FOOD ALLERGEN

=> dup remove l2
PROCESSING COMPLETED FOR L2
L3             7 DUP REMOVE L2 (12 DUPLICATES REMOVED)

=> d l3 1-7 cbib abs

L3   ANSWER 1 OF 7  CAPLUS  COPYRIGHT 2005 ACS on STN
2005:563471  Document No. 143:76843  Immunotherapy for food allergy by reduced
     and alkylated food allergens.  Koppelman, Stefan
     Johan; Penninks, Andreas Hendrikus; Knippels, Leon Mathieu Johannes
     (Nederlandse Organisatie Voor Toegepast-Natuurwetenschappelijk Onderzoek
     Tno, Neth.).  Eur. Pat. Appl. EP 1547610 A1 20050629, 16 pp.  DESIGNATED
     STATES: R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC,
     PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK.
     (English).  CODEN: EPXXDW.  APPLICATION: EP 2003-79161 20031223.
AB   The authors disclose treatment of individuals suffering from food allergy
     based on immunotherapy employing modified allergens.
     The allergens are derived from a dietary protein, preferably a tree nut
     protein and are modified by reduction and alkylation.  In one example, the
     modified protein is 2S albumin of Brazil nuts.

L3   ANSWER 2 OF 7  EMBASE  COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.
```

on STN
2004436030 EMBASE Vaccination with genetically engineered allergens prevents progression of allergic disease. Niederberger V.; Horak F.; Vrtala S.; Spitzauer S.; Krauth M.-T.; Valent P.; Reisinger J.; Pelzmann M.; Hayek B.; Kronqvist M.; Gafvelin G.; Gronlund H.; Purohit A.; Suck R.; Fiebig H.; Cromwell O.; Pauli G.; Van Hage-Hamsten M.; Valenta R.. R. Valenta, Department of Pathophysiology, Vienna General Hospital, University of Vienna, 1090 Vienna, Austria. rudolf.valenta@meduniwien.ac.at. Proceedings of the National Academy of Sciences of the United States of America Vol. 101, No. SUPPL. 2, pp. 14677-14682 5 Oct 2004.
Refs: 31.
ISSN: 0027-8424. CODEN: PNASA6
Pub. Country: United States. Language: English. Summary Language: English.
ED Entered STN: 20041112
AB IgE-mediated allergy affects >25% of the population in industrialized countries. Repeated contact with the disease-eliciting allergens induces rises of allergen-specific IgE Abs and progression of the disease to more severe manifestations. Our study uses a type of vaccine that is based on genetically **modified allergen** derivatives to treat allergic patients. We developed hypoallergenic derivatives of the major birch pollen allergen. Bet v 1, by genetic engineering and vaccinated birch pollen-allergic patients (n = 124) in a double-blind, placebo-controlled study. Active treatment induced protective IgG Abs that inhibited allergen-induced release of inflammatory mediators. We also observed a reduction of cutaneous sensitivity as well as an improvement of symptoms in actively treated patients. Most important, rises of allergen-specific IgE induced by seasonal birch pollen exposure were significantly reduced in vaccinated patients. Vaccination with genetically engineered allergen derivatives is a therapy for allergy that not only ameliorates allergic reactions but also reduces the IgE production underlying the disease.

L3 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
2003:855391 Document No. 139:363577 Modified anaphylactic **food allergens** with reduced IgE-binding ability for decreasing clinical reaction to allergy. Caplan, Michael J.; Sosin, Howard B.; Sampson, Hugh; Bannon, Gary A.; Burks, A. Wesley; Cockrell, Gael; Compadre, Cesar M.; Connaughton, Cathie; Helm, Ricki M.; King, Nina E.; Kopper, Randall A.; Maleki, Soheila J.; Rabjohn, Patrick A.; Shin, David S.; Stanley, J. Steven (USA). U.S. Pat. Appl. Publ. US 2003202980 A1 20031030, 194 pp., Cont.-in-part of U.S. Ser. No. 494,096. (English). CODEN: USXXCO. APPLICATION: US 2002-100303 20020318. PRIORITY: US 95-PV9455; 19951229; US 96-717933; 19960923; US 98-PV73283; 19980131; US 98-PV74633; 19980213; US 98-PV74624; 19980213; US 98-PV74590; 19980213; US 98-106872; 19980629; US 98-141220; 19980827; US 98-191593; 19981113; US 99-241101; 19990129; US 99-240557; 19990129; US 99-248674; 19990211; US 99-248673; 19990211; US 99-PV122560; 19990302; US 99-PV122565; 19990302; US 99-PV122566; 19990302; US 99-PV122450; 19990302; US 99-PV122452; 19990302; US 99-267719; 19990311; US 2000-2000/494096; 20000128.
AB It has been determined that allergens, which are characterized by both humoral (IgE) and cellular (T-cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by altering as little as a single amino acid within the protein, preferably a hydrophobic residue towards the center of the IgE epitope, to eliminate IgE binding. Addnl. or alternatively a **modified allergen** with reduced IgE binding may be prepared by disrupting one or more of the disulfide bonds that are present in the natural allergen. The disulfide bonds may be disrupted chemical, e.g., by reduction and alkylation or by mutating one or more cysteine residues present in the primary amino acid sequence of the natural allergen. In certain embodiments, **modified allergens** are prepared by both altering one or more linear IgE epitopes and disrupting one or more disulfide bonds of the natural allergen. In certain embodiments, the methods of the present invention

allow allergens to be modified while retaining the ability of the protein to activate T-cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The immunotherapeutics can be prepared in transgenic plants or animals; and administered in injection, aerosol, sublingual or topical form. The immunotherapeutics can also be encoded in gene for gene therapy and delivered by injecting into muscle or skin to induce tolerance. The Examples provided herein use peanut allergens to illustrate applications of the invention.

L3 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN
2003:906632 Correction of: 2002:736063 Document No. 139:349665 Correction of: 137:277814 Modified anaphylactic **food allergens** with reduced IgE-binding ability for decreasing clinical reaction to allergy. Caplan, Michael; Sosin, Howard; Sampson, Hugh; Bannon, Gary A.; Burks, Wesley A.; Cockrell, Gael; Compadre, Cesar M.; Connaughton, Cathie; Helm, Ricki M.; King, Nina E.; Kopper, Randall A.; Maleki, Sohelia J.; Rabjohn, Patrick A.; Shin, David S.; Stanley, J. Steven (Panacea Pharmaceuticals, USA; et al.). PCT Int. Appl. WO 2002074250 A2 20020926, 299 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US9108 20020318. PRIORITY: US 2001-2001/PV276822 20010316.

AB It has been determined that allergens, which are characterized by both humoral (IgE) and cellular (T-cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by altering as little as a single amino acid within the protein, preferably a hydrophobic residue towards the center of the IgE epitope, to eliminate IgE binding. Addnl. or alternatively a **modified allergen** with reduced IgE binding may be prepared by disrupting one or more of the disulfide bonds that are present in the natural allergen. The disulfide bonds may be disrupted chemical, e.g., by reduction and alkylation or by mutating one or more cysteine residues present in the primary amino acid sequence of the natural allergen. In certain embodiments, **modified allergens** are prepared by both altering one or more linear IgE epitopes and disrupting one or more disulfide bonds of the natural allergen. In certain embodiments, the methods of the present invention allow allergens to be modified while retaining the ability of the protein to activate T-cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The Examples provided herein use peanut allergens to illustrate applications of the invention.

L3 ANSWER 5 OF 7 MEDLINE on STN DUPLICATE 1
2002680648. PubMed ID: 12440942. Clinical aspects of food allergy. Papageorgiou P S. (Athens University School of Medicine, P & A. Kyriakou Children's Hospital, Allergy Unit, Greece 115 27.. phspapa@yahoo.com) . Biochemical Society transactions, (2002 Nov) 30 (Pt 6) 901-6. Ref: 36. Journal code: 7506897. ISSN: 0300-5127. Pub. country: England: United Kingdom. Language: English.

AB Food allergy affects 2.5% of adults and 6-8% of children, and is a leading cause of life-threatening anaphylactic episodes. Food allergy is defined as an adverse reaction to foods that is mediated immunologically and involves specific IgE or non-IgE mechanisms. In this review only IgE-related food allergy will be considered. Many **food allergens** are glycoproteins, but they do not share any striking biochemical similarities. The definition of many food proteins at the molecular level has tremendously facilitated our understanding of clinical syndromes and seemingly bizarre observations. Clinical manifestations of food allergy include symptoms of the gastrointestinal, cutaneous and

respiratory systems, as well as systemic anaphylaxis. The diagnosis of food allergy involves a stepwise approach, including medical history taking, demonstration of specific IgE and confirmation by oral food challenge. The management of the food-allergic patient at present consists of avoidance of the culprit food and education, while future advances may include specific immunotherapy with **modified allergens** or DNA vaccination.

L3 ANSWER 6 OF 7 MEDLINE on STN DUPLICATE 2

2000290936. PubMed ID: 10828721. Modulation of allergen-specific immune responses to the major shrimp allergen, tropomyosin, by specific targeting to scavenger receptors on macrophages. Rajagopal D; Ganesh K A; Subba Rao P V. (Department of Biochemistry, Indian Institute of Science, Bangalore, India.) International archives of allergy and immunology, (2000 Apr) 121 (4) 308-16. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: Tropomyosin from shrimp is the major cross-reacting crustacean **food allergen.** Earlier studies have led to the purification and immunochemical characterization of the major IgE binding epitopes of the allergen. Maleylated proteins are known to be specifically targeted to scavenger receptors on macrophage. Since antigens processed and presented by macrophages are known to elicit Th1 type of responses and allergic responses are characterized by polarization towards Th2 phenotype, the possibility of modulation of allergen-specific immune responses by targeting of tropomyosin to macrophage via scavenger receptor was explored. METHODS: The IgG and IgE binding potential of the native maleylated form of tropomyosin was carried out by ELISA and immunoblot. The ability of the native and maleylated form of allergen to induce in vitro proliferation of splenocytes from BALB/C mice immunized with both forms of allergen was tested. The in vitro production of IL-4 and IFN-gamma by splenocytes from mice immunized with the two forms of allergen was determined from culture supernatants. The in vivo production of serum IgG1 and IgG2a antibodies following immunization with native and **modified allergens** was monitored by ELISA. RESULTS: The maleylated form of tropomyosin was found to have reduced antigenicity and allergenicity as compared to its native counterpart. The **modified allergen** was, however, found to elicit a cellular response similar to native tropomyosin in vitro. Analysis of the cytokine profiles showed a modulation from an IL-4-dominant, proallergic, Th2 phenotype to an IFN-gamma-dominant, antiallergic, Th1 phenotype that could also be correlated to a modulation in the in vivo antibody isotype. CONCLUSION: The results suggest the possible potential for modulating allergic responses in vivo by selective targeting to macrophages.

L3 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 3

96282031. PubMed ID: 8721522. Monomeric chemically **modified allergens**: immunologic and physicochemical characterization. Mistrello G; Brenna O; Roncarolo D; Zanoni D; Gentili M; Falagiani P. (Department of Research, Laboratorio Famacautico Lofarma, Milan, Italy.) Allergy, (1996 Jan) 51 (1) 8-15. Journal code: 7804028. ISSN: 0105-4538. Pub. country: Denmark. Language: English.

AB Allergenic extracts (Der p, grass, and Parietaria) or single allergens such as Par j I (the major allergen of Parietaria) and ovalbumin (OA), a **food allergen** widely used in animal models, were chemically modified by reaction with potassium cyanate (KCNO), which transforms the epsilon-amino group of the lysine of proteinaceous allergens into ureido groups. KCNO-modified (carbamylated) allergens have low allergenic potency, as demonstrated in vitro (RAST inhibition) and in vivo (passive cutaneous anaphylaxis). When used to immunize rabbits, carbamylated allergens still induce IgG antibodies able to cross-react with native allergens (immunoblotting experiments). An interesting feature distinguishing carbamylated allergens from other chemically **modified allergens** is the preservation of the native monomeric dimension as demonstrated by SDS-PAGE analysis. Results are

discussed from the perspective of clinical application of carbamylated allergens.

=> s l1 and peant allergen
L4 0 L1 AND PEANT ALLERGEN

=> s l1 and peanut allergen
L5 11 L1 AND PEANUT ALLERGEN

=> dup reomve l5
ENTER REMOVE, IDENTIFY, ONLY, OR (?): remove
'REOMVE' IS NOT VALID. VALID FILE NAMES ARE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS'
You have entered a file name of duplicates to keep that is not referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.

=> dup remove l5
PROCESSING COMPLETED FOR L5
L6 6 DUP REMOVE L5 (5 DUPLICATES REMOVED)

=> d l6 1-6 cbib abs

L6 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
2003:855391 Document No. 139:363577 Modified anaphylactic food allergens with reduced IgE-binding ability for decreasing clinical reaction to allergy. Caplan, Michael J.; Sosin, Howard B.; Sampson, Hugh; Bannon, Gary A.; Burks, A. Wesley; Cockrell, Gael; Compadre, Cesar M.; Connaughton, Cathie; Helm, Ricki M.; King, Nina E.; Kopper, Randall A.; Maleki, Soheila J.; Rabjohn, Patrick A.; Shin, David S.; Stanley, J. Steven (USA). U.S. Pat. Appl. Publ. US 2003202980 A1 20031030, 194 pp., Cont.-in-part of U.S. Ser. No. 494,096. (English). CODEN: USXXCO. APPLICATION: US 2002-100303 20020318. PRIORITY: US 95-PV9455; 19951229; US 96-717933; 19960923; US 98-PV73283; 19980131; US 98-PV74633; 19980213; US 98-PV74624; 19980213; US 98-PV74590; 19980213; US 98-106872; 19980629; US 98-141220; 19980827; US 98-191593; 19981113; US 99-241101; 19990129; US 99-240557; 19990129; US 99-248674; 19990211; US 99-248673; 19990211; US 99-PV122560; 19990302; US 99-PV122565; 19990302; US 99-PV122566; 19990302; US 99-PV122450; 19990302; US 99-PV122452; 19990302; US 99-267719; 19990311; US 2000-2000/494096; 20000128.
AB It has been determined that allergens, which are characterized by both humoral (IgE) and cellular (T-cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by altering as little as a single amino acid within the protein, preferably a hydrophobic residue towards the center of the IgE epitope, to eliminate IgE binding. Addnl. or alternatively a **modified allergen** with reduced IgE binding may be prepared by disrupting one or more of the disulfide bonds that are present in the natural allergen. The disulfide bonds may be disrupted chemical, e.g., by reduction and alkylation or by mutating one or more cysteine residues present in the primary amino acid sequence of the natural allergen. In certain embodiments, **modified allergens** are prepared by both altering one or more linear IgE epitopes and disrupting one or more disulfide bonds of the natural allergen. In certain embodiments, the methods of the present invention allow allergens to be modified while retaining the ability of the protein to activate T-cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The immunotherapeutics can be prepared in transgenic plants or animals; and administered in injection, aerosol, sublingual or topical form. The immunotherapeutics can also be encoded in gene for gene therapy and delivered by injecting into muscle or skin to induce tolerance. The Examples provided herein use **peanut**

allergens to illustrate applications of the invention.

L6 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 1
2003:906632 Correction of: 2002:736063 Document No. 139:349665 Correction of: 137:277814 Modified anaphylactic food allergens with reduced IgE-binding ability for decreasing clinical reaction to allergy. Caplan, Michael; Sosin, Howard; Sampson, Hugh; Bannon, Gary A.; Burks, Wesley A.; Cockrell, Gael; Compadre, Cesar M.; Connaughton, Cathie; Helm, Ricki M.; King, Nina E.; Kopper, Randall A.; Maleki, Sohelia J.; Rabjohn, Patrick A.; Shin, David S.; Stanley, J. Steven (Panacea Pharmaceuticals, USA; et al.). PCT Int. Appl. WO 2002074250 A2 20020926, 299 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US9108 20020318. PRIORITY: US 2001-2001/PV276822 20010316.

AB It has been determined that allergens, which are characterized by both humoral (IgE) and cellular (T-cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by altering as little as a single amino acid within the protein, preferably a hydrophobic residue towards the center of the IgE epitope, to eliminate IgE binding. Addnl. or alternatively a **modified allergen** with reduced IgE binding may be prepared by disrupting one or more of the disulfide bonds that are present in the natural allergen. The disulfide bonds may be disrupted chemical, e.g., by reduction and alkylation or by mutating one or more cysteine residues present in the primary amino acid sequence of the natural allergen. In certain embodiments, **modified allergens** are prepared by both altering one or more linear IgE epitopes and disrupting one or more disulfide bonds of the natural allergen. In certain embodiments, the methods of the present invention allow allergens to be modified while retaining the ability of the protein to activate T-cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The Examples provided herein use **peanut allergens** to illustrate applications of the invention.

L6 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
2002:301398 Document No.: PREV200200301398. Immunotherapy for peanut allergy using **modified allergens** and a bacterial adjuvant.
Stanley, Joseph Steve [Reprint author]; Buzen, Fred [Reprint author]; Cockrell, Gael [Reprint author]; West, Mike [Reprint author]; Srivastava, Kamal D.; Li, X. M.; Sampson, Hugh A.; Burks, Wesley [Reprint author]; Bannon, Gary A. [Reprint author]. University of Arkansas, Little Rock, AR, USA. Journal of Allergy and Clinical Immunology, (January, 2002) Vol. 109, No. 1 Supplement, pp. S93. print.
Meeting Info.: 58th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. New York, NY, USA. March 01-06, 2002. American Academy of Allergy, Asthma, and Immunology.
CODEN: JACIBY. ISSN: 0091-6749. Language: English.

L6 ANSWER 4 OF 6 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN
2002:530650 The Genuine Article (R) Number: 563MD. Modification of **peanut allergen** Ara h 3: Effects on IgE binding and T cell stimulation. Rabjohn P; West C M; Connaughton C; Sampson H A; Helm R M (Reprint); Burks A W; Bannon G A. Univ Arkansas Med Sci, ACHRI, Dept Biochem & Mol Biol, Slot 512, 1120 Marshall St, Little Rock, AR 72202 USA (Reprint); Univ Arkansas Med Sci, ACHRI, Dept Biochem & Mol Biol, Little Rock, AR 72202 USA; Univ Arkansas Med Sci, ACHRI, Dept Pediat, Little

Rock, AR 72202 USA; Mt Sinai Sch Med, Dept Pediat, New York, NY USA. INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY (MAY 2002) Vol. 128, No. 1, pp. 15-23. ISSN: 1018-2438. Publisher: KARGER, ALLSCHWILERSTRASSE 10, CH-4009 BASEL, SWITZERLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background: Peanut allergy is a major health concern due to the increased prevalence, potential severity, and chronicity of the reaction. The cDNA encoding a third **peanut allergen**, Ara h 3, has been previously cloned and characterized. Mutational analysis of the Ara h 3 IgE-binding epitopes with synthetic peptides revealed that single amino acid changes at critical residues could diminish IgE binding. Methods: Specific oligonucleotides were used in polymerase chain reactions to modify the cDNA encoding Ara h 3 at critical IgE binding sites. Four point mutations were introduced into the Ara h 3 cDNA at codons encoding critical amino acids in epitopes 1, 2, 3 and 4. Recombinant modified proteins were used in SDS-PAGE/Western IgE immunoblot, SDS-PAGE/Western IgE immunoblot inhibition and T cell proliferation assays to determine the effects of these changes on in vitro clinical indicators of peanut hypersensitivity. Results: Higher amounts of modified Ara h 3 were required to compete with the wild-type allergen for peanut-specific serum IgE. Immunoblot analysis with individual serum IgE from Ara-h-3-allergic patients showed that IgE binding to the modified protein decreased similar to35-85% in comparison to IgE binding to wildtype Ara h 3. Also, the modified Ara h 3 retained the ability to stimulate T cell activation in PBMCs donated by Ara-h-3-allergic patients. Conclusions: The engineered hypoallergenic Ara h 3 variant displays two characteristics essential for recombinant allergen immunotherapy; it has a reduced binding capacity for serum IgE from peanut-hypersensitive patients and it can stimulate T-cell proliferation and activation. Copyright (C) 2002 S, Karger AG, Basel.

L6 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 2

2001262411. PubMed ID: 11306930. Engineering, characterization and in vitro efficacy of the major **peanut allergens** for use in immunotherapy. Bannon G A; Cockrell G; Connaughton C; West C M; Helm R; Stanley J S; King N; Rabjohn P; Sampson H A; Burks A W. (Department of Biochemistry and Molecular Biology, Arkansas Children's Hospital Research Institute, Little Rock 72205, USA.. bannongarya@exchnage.uams.edu) . International archives of allergy and immunology, (2001 Jan-Mar) 124 (1-3) 70-2. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: Numerous strategies have been proposed for the treatment of peanut allergies, but despite the steady advancement in our understanding of atopic immune responses and the increasing number of deaths each year from peanut anaphylaxis, there is still no safe, effective, specific therapy for the peanut-sensitive individual. Immunotherapy would be safer and more effective if the allergens could be altered to reduce their ability to initiate an allergic reaction without altering their ability to desensitize the allergic patient. METHODS: The cDNA clones for three major **peanut allergens**, Ara h 1, Ara h 2, and Ara h 3, have been cloned and characterized. The IgE-binding epitopes of each of these allergens have been determined and amino acids critical to each epitope identified. Site-directed mutagenesis of the allergen cDNA clones, followed by recombinant production of the **modified allergen**, provided the reagents necessary to test our hypothesis that hypoallergenic proteins are effective immunotherapeutic reagents for treating peanut-sensitive patients. Modified **peanut allergens** were subjected to immunoblot analysis using peanut-positive patient sera IgE, T cell proliferation assays, and tested in a murine model of peanut anaphylaxis. RESULTS: In general, the **modified allergens** were poor competitors for binding of peanut-specific IgE when compared to their wild-type counterpart. The **modified allergens** demonstrated a greatly reduced IgE-binding capacity when individual patient serum IgE was compared to the binding capacity of the wild-type allergens. In addition, while there was considerable variability between patients, the **modified**

allergens retained the ability to stimulate T cell proliferation. CONCLUSIONS: These **modified allergen** genes and proteins should provide a safe immunotherapeutic agent for the treatment of peanut allergy.
Copyright 2001 S. Karger AG, Basel

L6 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
1999:495393 Document No. 131:143513 Methods and reagents for decreasing allergic reactions. Sosin, Howard; Bannon, Gary A.; Burks, A. Wesley, Jr.; Sampson, Hugh A. (University of Arkansas, USA; Mt. Sinai School of Medicine, University of New York). PCT Int. Appl. WO 9938978 A1 19990805, 46 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US2031 19990129. PRIORITY: US 1998-PV73283 19980131; US 1998-PV74590 19980213; US 1998-PV74624 19980213; US 1998-PV74633 19980213; US 1998-141220 19980827.
AB It has been determined that allergens, which are characterized by both humoral (IgE) and cellular (T cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by masking the site with a compound that prevents IgE binding or by altering as little as a single amino acid within the protein, most typically a hydrophobic residue towards the center of the IgE-binding epitope, to eliminate IgE binding. The method allows the protein to be altered as minimally as possible, other than within the IgE-binding sites, while retaining the ability of the protein to activate T cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The examples use **peanut allergens** to demonstrate alteration of IgE binding sites. The critical amino acids within each of the IgE binding epitopes of the peanut protein that are important to Ig binding have been determined Substitution of even a single amino acid within each of the epitopes led to loss of IgE binding. Although the epitopes shared no common amino acid sequence motif, the hydrophobic residues located in the center of the epitope appeared to be most critical to IgE binding.

```
=> s l1 and "E coli"
L7            0 L1 AND "E COLI"

=> d his

     (FILE 'HOME' ENTERED AT 15:52:18 ON 02 SEP 2005)

     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 15:52:30 ON
     02 SEP 2005
L1          464 S MODIFIED ALLERGEN
L2           19 S L1 AND FOOD ALLERGEN
L3            7 DUP REMOVE L2 (12 DUPLICATES REMOVED)
L4            0 S L1 AND PEANT ALLERGEN
L5           11 S L1 AND PEANUT ALLERGEN
L6            6 DUP REMOVE L5 (5 DUPLICATES REMOVED)
L7            0 S L1 AND "E COLI"

=> s l1 and expression
L8           10 L1 AND EXPRESSION

=> dup remove l8
PROCESSING COMPLETED FOR L8
L9            7 DUP REMOVE L8 (3 DUPLICATES REMOVED)
```

=> d l9 1-7 cbib abs

L9 ANSWER 1 OF 7 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

2003:546621 The Genuine Article (R) Number: 693QZ. Analysis of the CD4(+) T cell responses to house dust mite allergoid. Kalinski P; Lebre M C; Kramer D; de Jong E C; van Schijndel J W P M; Kapsenberg M L (Reprint). Univ Amsterdam, Acad Med Ctr, Dept Cell Biol & Histol, POB 22700, NL-1100 DE Amsterdam, Netherlands (Reprint); Univ Amsterdam, Acad Med Ctr, Dept Cell Biol & Histol, NL-1100 DE Amsterdam, Netherlands; Univ Amsterdam, Acad Med Ctr, Dept Dermatol, NL-1105 AZ Amsterdam, Netherlands; Haarlems Allergenen Lab, Haarlem, Netherlands. ALLERGY (JUL 2003) Vol. 58, No. 7, pp. 648-656. ISSN: 0105-4538. Publisher: BLACKWELL MUNKSGAARD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Background: **Modified allergen** extracts (allergoids) with reduced IgE-binding capacity are successfully used in immunotherapy of atopic allergy. Their reduced T-cell stimulatory capacity is less well studied and is a subject of the present study.

Methods: We compared the ability of native house dust mite extract (Dermatophagoides pteronyssinus ; HDM) and the glutaraldehyde-modified allergoid (HDM-GA) to induce the proliferation and cytokine production by fresh PBMC and by DC-stimulated polyclonal Th cells and HDM-specific Th cell clones.

Results: Freshly isolated T cells showed a partially reduced responsiveness to HDM-GA, differentially pronounced in different donors. HDM-specific Th cell clones prepared from three donors showed either a complete loss of reactivity to HDM-GA, or completely preserved responsiveness. The frequency of nonreactive clones was donor-dependent (2/3, 3/10 and 1/10). GA modification of HDM did not interfere with the cytokine production profile of HDM-specific T cell clones.

Conclusions: The reduced stimulatory potential of HDM-GA results mainly from a loss of certain Th cell epitopes, rather than impaired allergen uptake and presentation, or induction of suppressive factors. Varying frequencies of allergoid-nonreactive HDM-specific Th cells may result in differential responses of individual patients to immunotherapy.

L9 ANSWER 2 OF 7 CAPLUS COPYRIGHT 2005 ACS on STN

2001:320966 Document No. 135:225746 Allergenicity of hybrid Ag 5s of yellow jacket and paper wasp venoms. King, T. P.; Kagey-Sobotka, A.; Jim, S.; Monsalve, R. I.; Lichtenstein, L. M.; Spangfort, M. D. (School of Medicine and ALK-Abello, Rockefeller University, Johns Hopkins University, New York, NY, 10021-6399, USA). International Archives of Allergy and Immunology, 124(1-3), 85-86 (English) 2001. CODEN: IAAIEG. ISSN: 1018-2438. Publisher: S. Karger AG.

AB Antigen (Ag) 5 is a major allergen of vaspid venoms. Homologous Ag 5s from yellow jacket (Vespula vulgaris) and paper wasp (Polistes annularis) have 59% sequence identity of their resp. 204- and 205-amino acid residues. These two Ag 5s, designated as Ves v 5 and Pol a 5, resp., have low degrees of antigenic cross-reactivity in insect-allergic patients and in animal models. The structure of Ves v 5 has been recently solved by x-ray crystallog. A study was conducted in which hybrids containing different segments of these two vespid Ag 5s were prepared by **expression** in yeast to study their immunol. properties. Findings illustrate that hybrid allergens can have a 100- to a 1000-fold reduction in allergenicity, yet retaining the immunogenicity of the natural allergens. This reduction in allergenicity of hybrids is due to a decrease of B cell epitope d. Each of the hybrids studied has only a portion of the B and T cell epitopes of Ves v 5, and a mixture of the hybrids can, in principle, reconstitute the complete epitope library. Thus, this may be a useful approach to prepare **modified allergens** for use as vaccines as many allergens have sequence homol. with proteins from other sources.

L9 ANSWER 3 OF 7 MEDLINE on STN

2000290936. PubMed ID: 10828721. Modulation of allergen-specific immune

responses to the major shrimp allergen, tropomyosin, by specific targeting to scavenger receptors on macrophages. Rajagopal D; Ganesh K A; Subba Rao P V. (Department of Biochemistry, Indian Institute of Science, Bangalore, India.) International archives of allergy and immunology, (2000 Apr) 121 (4) 308-16. Journal code: 9211652. ISSN: 1018-2438. Pub. country: Switzerland. Language: English.

AB BACKGROUND: Tropomyosin from shrimp is the major cross-reacting crustacean food allergen. Earlier studies have led to the purification and immunochemical characterization of the major IgE binding epitopes of the allergen. Maleylated proteins are known to be specifically targeted to scavenger receptors on macrophage. Since antigens processed and presented by macrophages are known to elicit Th1 type of responses and allergic responses are characterized by polarization towards Th2 phenotype, the possibility of modulation of allergen-specific immune responses by targeting of tropomyosin to macrophage via scavenger receptor was explored. METHODS: The IgG and IgE binding potential of the native maleylated form of tropomyosin was carried out by ELISA and immunoblot. The ability of the native and maleylated form of allergen to induce in vitro proliferation of splenocytes from BALB/C mice immunized with both forms of allergen was tested. The in vitro production of IL-4 and IFN-gamma by splenocytes from mice immunized with the two forms of allergen was determined from culture supernatants. The in vivo production of serum IgG1 and IgG2a antibodies following immunization with native and **modified allergens** was monitored by ELISA. RESULTS: The maleylated form of tropomyosin was found to have reduced antigenicity and allergenicity as compared to its native counterpart. The **modified allergen** was, however, found to elicit a cellular response similar to native tropomyosin in vitro. Analysis of the cytokine profiles showed a modulation from an IL-4-dominant, proallergic, Th2 phenotype to an IFN-gamma-dominant, antiallergic, Th1 phenotype that could also be correlated to a modulation in the in vivo antibody isotype. CONCLUSION: The results suggest the possible potential for modulating allergic responses in vivo by selective targeting to macrophages.

L9 ANSWER 4 OF 7 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

1998:917772 The Genuine Article (R) Number: 144YJ. Long-term analysis of allergen-specific T cell clones from patients with asthma treated with allergen rush immunotherapy. Oda N (Reprint); Yamashita N; Minoguchi K; Takeno M; Kaneko S; Sakane T; Adachi M. Showa Univ, Dept Internal Med 1, Tokyo 142, Japan (Reprint); St Marianna Univ, Sch Med, Dept Immunol, Kanagawa, Japan; St Marianna Univ, Sch Med, Dept Med, Kanagawa, Japan. CELLULAR IMMUNOLOGY (25 NOV 1998) Vol. 190, No. 1, pp. 43-50. ISSN: 0008-8749. Publisher: ACADEMIC PRESS INC, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Rush immunotherapy (RI), a **modified allergen** -specific immunotherapeutic procedure, is an effective treatment for extrinsic (atopic) asthma, although the precise mechanism of its action is unclear. We have thus investigated the effect of RI on T cell response in seven mite-allergen-sensitive asthmatic patients who were successfully treated with RI. The proliferative response to mite allergen profoundly decreased after 3 months of therapy compared to the response before therapy; the response, however, recovered 18 months after RI. Regarding cytokine production patterns of mite-specific T cells, RI brought about a shift in cytokine profiles from Th2 to Th0 or Th1 in mite-specific T cell clones. The data indicate that the efficacy of RI is due to modification of T cell responses to mite antigens. Allergen RI results in the conversion of Th2 to Th1 and Th0 cells and/or selection of Th1 and Th0 cells over Th2 cells and thus may improve both clinical symptoms and airway inflammation in asthmatics. (C) 1998 Academic Press.

L9 ANSWER 5 OF 7 MEDLINE on STN

93107727. PubMed ID: 7678032. Allergen-specific modulation of cytokine

synthesis patterns and IgE responses in vivo with chemically **modified allergen.** Gieni R S; Yang X; HayGlass K T. (Department of Immunology, University of Manitoba, Winnipeg, Canada.) Journal of immunology (Baltimore, Md. : 1950), (1993 Jan 1) 150 (1) 302-10. Journal code: 2985117R. ISSN: 0022-1767. Pub. country: United States. Language: English.

AB Hypersensitivity and IgE synthesis are highly dependent on the balance in which production of IL-4 and IFN-gamma is induced. An immunologic approach that alters the dominant pattern of cytokine synthesis and antibody production that is elicited after exposure to native allergen is described. High M(r), glutaraldehyde-polymerized OVA administered (i.p.) before or after immunization with unmodified OVA induces > or = 95% inhibition of specific IgE synthesis concomitant with 300- to 800-fold increases in IgG2a production in C57BL/6 mice. These changes result from a genetically controlled shift in the pattern of cytokine production within the allergen-specific T cell repertoire as demonstrated by i) susceptibility of the changes induced upon administration of **modified allergen** to in vivo treatment with anti-IFN-gamma mAb and ii) a 5- to 7-fold increase in the ratio of IFN-gamma:IL-4 synthesis after overnight culture directly ex vivo. This system should prove useful in identification of the factors which are influential in the commitment of T cells to Th1- or Th2-like patterns of cytokine synthesis. Moreover, as defective induction of IFN-gamma by allergen-specific T cells appears to play a role in elevated IgE synthesis and human allergy, this approach may have therapeutic potential.

L9 ANSWER 6 OF 7 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

1992:371980 The Genuine Article (R) Number: HZ071. CHARACTERIZATION OF SUPPRESSOR T-CELL CLONES DERIVED FROM A MOUSE TOLERIZED WITH CONJUGATES OF OVALBUMIN AND MONOMETHOXYPOLYETHYLENE GLYCOL. CHEN Y H (Reprint); TAKATA M; MAITI P K; RECTOR E S; SEHON A H. UNIV MANITOBA, DEPT IMMUNOL, ALLERGY RES GRP, MRC, WINNIPEG R3E 0W3, MANITOBA, CANADA (Reprint). CELLULAR IMMUNOLOGY (JUN 1992) Vol. 142, No. 1, pp. 16-27. ISSN: 0008-8749. Publisher: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495. Language: English.

L9 ANSWER 7 OF 7 MEDLINE on STN DUPLICATE 1

90316167. PubMed ID: 2142456. Allergen-directed **expression** of Fc receptors for IgE (CD23) on human T lymphocytes is modulated by interleukin 4 and interferon-gamma. Prinz J C; Baur X; Mazur G; Rieber E P. (Institute for Immunology, Ludwig-Maximilians-University, Munich, FRG.) European journal of immunology, (1990 Jun) 20 (6) 1259-64. Journal code: 1273201. ISSN: 0014-2980. Pub. country: GERMANY, WEST: Germany, Federal Republic of. Language: English.

AB T lymphocytes bearing Fc receptors (FcR) for immunoglobulins are known to have immunoglobulin class-specific regulatory functions. Here we report that **expression** on T cells of the low-affinity FcR for IgE (Fc epsilon RII/CD23) is preferentially induced by stimulation with antigens that cause an IgE response. T cells from eight patients allergic to the hemoglobin of Chironomus thummi thummi mosquito larvae (CHIT I) were analyzed for reactivity with the anti-FcERII/CD23 monoclonal antibody (mAb) M-L25 under various conditions. No Fc epsilon RII/CD23+ T cells were observed among freshly isolated, resting peripheral blood mononuclear cells (PBMC). Stimulation of PBMC with CHIT I, however, induced a marked although transient Fc epsilon RII/CD23 **expression** on a large portion of the allergen-activated T lymphocytes. It reached a maximum of 37.2 +/- 4.6% Fc epsilon RII/CD23+ T cell blasts on day 5 of culture. The selectivity of this **expression** became evident when compared to non-allergenic control antigens: after stimulation of PBMC with tetanus toxoid or purified protein derivative from tuberculin a maximum of 4.6% +/- 1.4% and 4.2% +/- 1.1% T cell blasts was found to express Fc epsilon RII/CD23, respectively. Activation by an anti-CD3 mAb was insufficient to induce Fc epsilon RII/CD23 on T cells. The allergen-stimulated Fc epsilon RII/CD23+ T cells exclusively belonged to the CD4+CD29+ helper inducer T

cell subset. Using a cDNA probe coding for the B cell Fc epsilon RII/CD23, Northern blot analysis revealed a 1.7-kb Fc epsilon RII/CD23 mRNA in extracts of highly purified allergen-stimulated T cells. It was of the same size as Fc epsilon RII/CD23 mRNA of the lymphoblastoid B cell line WI-L2. Of several cytokines tested [interleukin (IL) 1 to IL 6, interferon-gamma (IFN-gamma), tumor necrosis factor-alpha] only IL 4 and IFN-gamma significantly **modified allergen**-induced Fc epsilon RII/CD23 **expression** on T cells. The latter was enhanced nearly twofold in the presence of IL 4, and was almost completely abrogated by IFN-gamma. IL 4, however, could not increase the number of Fc epsilon RII/CD23+ T lymphocytes either alone or in combination with an anti-CD3 mAb. Taken together, the selective induction of Fc epsilon RII/CD23 on T cells by allergen and its inclusion in the regulatory network of cytokines point to an important role of Fc epsilon RII/CD23+ T lymphocytes in the human IgE response.

```
=> s peanut allergen
L10         881 PEANUT ALLERGEN

=> s l10 and modified
L11          44 L10 AND MODIFIED

=> s l11 and E coli
L12           8 L11 AND E COLI

=> dup remove l12
PROCESSING COMPLETED FOR L12
L13           2 DUP REMOVE L12 (6 DUPLICATES REMOVED)

=> d l13 1-2 cbib abs
```

L13 ANSWER 1 OF 2 MEDLINE on STN DUPLICATE 1
2003475502. PubMed ID: 14550644. High-yield expression in Escherichia coli, purification, and characterization of properly folded major **peanut allergen** Ara h 2. Lehmann Katrin; Hoffmann Silke; Neudecker Philipp; Suhr Martin; Becker Wolf-Meinhard; Rosch Paul. (Lehrstuhl Biopolymere, Universitat Bayreuth 30, Universitaetsstrasse 30, 95440, Bayreuth, Germany.) Protein expression and purification, (2003 Oct) 31 (2) 250-9. Journal code: 9101496. ISSN: 1046-5928. Pub. country: United States. Language: English.

AB Allergic reactions to peanuts are a serious health problem because of their high prevalence, associated with potential severity, and chronicity. One of the three major allergens in peanut, Ara h 2, is a member of the conglutin family of seed storage proteins. Ara h 2 shows high sequence homology to proteins of the 2S albumin family. Presently, only very few structural data from allergenic proteins of this family exist. For a detailed understanding of the molecular mechanisms of food-induced allergies and for the development of therapeutic strategies knowledge of the high-resolution three-dimensional structure of allergenic proteins is essential. We report a method for the efficient large-scale preparation of properly folded Ara h 2 for structural studies and report CD-spectroscopic data. In contrast to other allergenic 2S albumins, Ara h 2 exists as a single continuous polypeptide chain in peanut seeds, and thus heterologous expression in Escherichia coli was possible. Ara h 2 was expressed as Trx-His-tag fusion protein in **E. coli** Origami (DE3), a **modified E. coli** strain with oxidizing cytoplasm which allows the formation of disulfide bridges. It could be shown that recombinant Ara h 2, thus overexpressed and purified, and the allergen isolated from peanuts are identical as judged from immunoblotting, analytical HPLC, and circular dichroism spectra.

L13 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 2
2000417948. PubMed ID: 10910733. Use of **modified** BL21(DE3) Escherichia coli cells for high-level expression of recombinant

peanut allergens affected by poor codon usage.
Kleber-Janke T; Becker W M. (Department of Molecular and Biochemical Allergology, Research Center Borstel, Parkallee 22, Borstel, D-23845, Germany.. tamara.kleber_janke@gmx.de) . Protein expression and purification, (2000 Aug) 19 (3) 419-24. Journal code: 9101496. ISSN: 1046-5928. Pub. country: United States. Language: English.

AB We previously cloned a panel of **peanut allergens** by phage display technology. Examination of the codons used in these sequences indicated that most of the cDNAs contain an excess of the least used codons in Escherichia coli, namely AGG/AGA, that correspond to a minor tRNA, the product of the dnaY gene. To achieve high-level expression of the **peanut allergens**, the cDNAs were subcloned into an expression vector of the pET series (Novagen) in order to produce (His)(10)-tagged fusion proteins in conventional **E. coli** BL21(DE3) cells. The **peanut allergens** Ara h 1, Ara h 2, and Ara h 6 with an AGG/AGA codon content of 8-10% were only marginally expressed, whereas the peanut profilin Ara h 5, with an AGG/AGA codon content of only 0.8%, was efficiently expressed in these cells. Hence, by using **modified** BL21(DE3) **E. coli** cells, namely BL21-CodonPlus(DE3)-RIL cells (Stratagene) with extra copies of **E. coli** argU, ileY, and leuW tRNA genes, it was possible to attain high-level expression of the proteins affected by rare codon usage. IPTG-induced expression of several recombinant **peanut allergens**, such as Ara h 1, Ara h 2, and Ara h 6, was greatly increased in these special cells compared to the expression yield achieved by conventional **E. coli** hosts. The purification of the soluble and the insoluble fraction of Ara h 2 was performed by metal-affinity chromatography and yielded a total of about 30 mg (His)(10)-tagged recombinant protein per liter of culture of transformed BL21(DE3)CodonPlus-RIL cells. This is over 100 times more than achieved by production of Ara h 2 in conventional BL21(DE3) cells. Copyright 2000 Academic Press.

```
=> s (caplan m?/au)
L14       1353 (CAPLAN M?/AU)

=> s l14 and peanut
L15          8 L14 AND PEANUT

=> dup remove l15
PROCESSING COMPLETED FOR L15
L16          8 DUP REMOVE L15 (0 DUPLICATES REMOVED)

=> d l16 1-8 cbib abs

L16  ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2005 ACS on STN
2005:259357  Document No. 142:334946  Recombinant allergens with mutated IgE
     epitopes for treating anaphylaxis induced by food, venom, drug and latex
     allergens.  Caplan, Michael J.; Bottomly, Kim H.; Sosin, Howard
     B.; Burks, A. Wesley; Sampson, Hugh A. (USA).  U.S. Pat. Appl. Publ. US
     2005063994 A1 20050324, 117 pp., Cont.-in-part of U.S. Ser. No. 100,303.
     (English).  CODEN: USXXCO.  APPLICATION: US 2004-899551 20040726.
     PRIORITY: US 2000-2000/PV19503U 20000406; US 2000-2000/731375 20001206; US
     2002-2002/100303 20020318.
AB   The present invention provides methods and compns. for treating or
     preventing allergic reactions, particularly anaphylactic reactions.
     Methods of the present invention involve administering microorganisms to
     allergic subjects, where the microorganisms contain a recombinant version
     of the protein allergen.  The recombinant version can be wild-type or may
     include mutations within IgE epitopes of the protein allergen.  Preferably
     the compns. are administered rectally.  Particularly preferred
     microorganisms are bacteria such as E. coli .  Any allergen may be used in
     the inventive methods.  Particularly preferred allergens are anaphylactic
     allergens including protein allergens found in foods, venoms, drugs and
```

latex. The inventive compns. and methods are demonstrated in the treatment of **peanut**-induced anaphylaxis.

L16 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
2003:855391 Document No. 139:363577 Modified anaphylactic food allergens with reduced IgE-binding ability for decreasing clinical reaction to allergy. **Caplan, Michael J.**; Sosin, Howard B.; Sampson, Hugh; Bannon, Gary A.; Burks, A. Wesley; Cockrell, Gael; Compadre, Cesar M.; Connaughton, Cathie; Helm, Ricki M.; King, Nina E.; Kopper, Randall A.; Maleki, Soheila J.; Rabjohn, Patrick A.; Shin, David S.; Stanley, J. Steven (USA). U.S. Pat. Appl. Publ. US 2003202980 A1 20031030, 194 pp., Cont.-in-part of U.S. Ser. No. 494,096. (English). CODEN: USXXCO. APPLICATION: US 2002-100303 20020318. PRIORITY: US 95-PV9455; 19951229; US 96-717933; 19960923; US 98-PV73283; 19980131; US 98-PV74633; 19980213; US 98-PV74624; 19980213; US 98-PV74590; 19980213; US 98-106872; 19980629; US 98-141220; 19980827; US 98-191593; 19981113; US 99-241101; 19990129; US 99-240557; 19990129; US 99-248674; 19990211; US 99-248673; 19990211; US 99-PV122560; 19990302; US 99-PV122565; 19990302; US 99-PV122566; 19990302; US 99-PV122450; 19990302; US 99-PV122452; 19990302; US 99-267719; 19990311; US 2000-2000/494096; 20000128.
AB It has been determined that allergens, which are characterized by both humoral (IgE) and cellular (T-cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can be converted to non-IgE binding sites by altering as little as a single amino acid within the protein, preferably a hydrophobic residue towards the center of the IgE epitope, to eliminate IgE binding. Addnl. or alternatively a modified allergen with reduced IgE binding may be prepared by disrupting one or more of the disulfide bonds that are present in the natural allergen. The disulfide bonds may be disrupted chemical, e.g., by reduction and alkylation or by mutating one or more cysteine residues present in the primary amino acid sequence of the natural allergen. In certain embodiments, modified allergens are prepared by both altering one or more linear IgE epitopes and disrupting one or more disulfide bonds of the natural allergen. In certain embodiments, the methods of the present invention allow allergens to be modified while retaining the ability of the protein to activate T-cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The immunotherapeutics can be prepared in transgenic plants or animals; and administered in injection, aerosol, sublingual or topical form. The immunotherapeutics can also be encoded in gene for gene therapy and delivered by injecting into muscle or skin to induce tolerance. The Examples provided herein use **peanut** allergens to illustrate applications of the invention.

L16 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
2003:906632 Correction of: 2002:736063 Document No. 139:349665 Correction of: 137:277814 Modified anaphylactic food allergens with reduced IgE-binding ability for decreasing clinical reaction to allergy. **Caplan, Michael**; Sosin, Howard; Sampson, Hugh; Bannon, Gary A.; Burks, Wesley A.; Cockrell, Gael; Compadre, Cesar M.; Connaughton, Cathie; Helm, Ricki M.; King, Nina E.; Kopper, Randall A.; Maleki, Sohelia J.; Rabjohn, Patrick A.; Shin, David S.; Stanley, J. Steven (Panacea Pharmaceuticals, USA; et al.). PCT Int. Appl. WO 2002074250 A2 20020926, 299 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US9108 20020318. PRIORITY: US 2001-2001/PV276822 20010316.
AB It has been determined that allergens, which are characterized by both humoral (IgE) and cellular (T-cell) binding sites, can be modified to be less allergenic by modifying the IgE binding sites. The IgE binding sites can

be converted to non-IgE binding sites by altering as little as a single amino acid within the protein, preferably a hydrophobic residue towards the center of the IgE epitope, to eliminate IgE binding. Addnl. or alternatively a modified allergen with reduced IgE binding may be prepared by disrupting one or more of the disulfide bonds that are present in the natural allergen. The disulfide bonds may be disrupted chemical, e.g., by reduction and alkylation or by mutating one or more cysteine residues present in the primary amino acid sequence of the natural allergen. In certain embodiments, modified allergens are prepared by both altering one or more linear IgE epitopes and disrupting one or more disulfide bonds of the natural allergen. In certain embodiments, the methods of the present invention allow allergens to be modified while retaining the ability of the protein to activate T-cells, and, in some embodiments by not significantly altering or decreasing IgG binding capacity. The Examples provided herein use **peanut** allergens to illustrate applications of the invention.

L16 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

2001:676622 Document No. 135:225857 Microbial delivery system. **Caplan, Michael** (Panacea Pharmaceuticals, LLC, USA). PCT Int. Appl. WO 2001066136 A2 20010913, 57 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33121 20001206. PRIORITY: US 2000-PV195035 20000306.

AB The present invention provides methods and compns. for treating or preventing allergic responses, particularly anaphylactic allergic responses, in subjects who are allergic to allergens or susceptible to allergies. Methods of the present invention utilize administration of microorganisms to subjects, where the microorganisms produce allergens and protect the subjects from exposure to the allergens until phagocytosed by antigen-presenting cells. Particularly preferred microorganisms are gram-neg. bacteria, gram-pos. bacteria, and yeast. Particularly preferred allergens are proteins found in foods, venoms, drugs and latex that elicit allergic reactions and anaphylactic allergic reactions in individuals who are allergic to the proteins or are susceptible to allergies to the proteins. The proteins may also be modified to reduce the ability of the proteins to bind and crosslink IgE antibodies and thereby reduce the risk of eliciting anaphylaxis without affecting T-cell mediated Th1-type immunity.

L16 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

2001:416973 Document No. 135:45198 Prevention of an anaphylactic response to food allergens. Bannon, Gary A.; Burks, Wesley A.; **Caplan, Michael J.**; Sampson, Hugh; Sosin, Howard (Panacea Pharmaceuticals, LLC, USA; University of Arkansas; Mount Sinai School of Medicine, University of New York). PCT Int. Appl. WO 2001040264 A2 20010607, 100 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33124 20001206. PRIORITY: US 1999-455294 19991206; US 2000-PV213765 20000623; US 2000-PV235797 20000927.

AB The authors disclose methods for reducing allergic responses in individuals sensitive to one or more food antigens. In general, desensitization is achieved by administration of fragments of antigens

characterized by a reduced ability to bind to their cognate IgE. In one example, mice were sensitized to **peanut** allergens by intragastric feeding. Administration of peptide fragments of Ara h 2, or an allergen mutein with altered IgE binding sites, abrogated an increase in IgE levels and anaphylactic sequelae.

L16 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
2001:416792 Document No. 135:10056 Controlled delivery of antigens. **Caplan, Michael**; Burks, Wesley A., Jr.; Bannon, Gary A. (The Board of Trustees of the University of Arkansas, USA; Panacea Pharmaceuticals, LLC). PCT Int. Appl. WO 2001039800 A2 20010607, 34 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US42607 20001206. PRIORITY: US 1999-PV169330 19991206.

AB Formulations and methods are developed for delivering antigens to individuals in a manner that substantially reduces contact between the antigen and IgE receptors displayed on the surfaces of cells involved in mediating allergic responses, which target delivery of antigen to dendritic, phagocytic and antigen presenting cells (APCs), and which have improved pharmacokinetics. By reducing direct and indirect association of antigens with antigen-specific IgE antibodies, the risk of an allergic reaction, possibly anaphylactic shock, is reduced or eliminated. Particularly preferred antigens are those that may elicit anaphylaxis in individuals, including food antigens, insect venom and rubber-related antigens. In the preferred embodiments, the compns. include one or more antigens in a delivery material such as a polymer, in the form of particles or a gel, or lipid vesicles or liposomes, any of which can be stabilized or targeted to enhance delivery. Preferably, the antigen is surrounded by the encapsulation material. Alternatively or addnl., the antigen is displayed on the surface of the encapsulation material. One result of encapsulating antigen is the reduction in association with antigen-specific IgE antibodies. In some embodiments, antigens are stabilized or protected from degradation until the antigen can be recognized and endocytized by APCs which are involved in eliciting cellular and humoral immune responses. In a preferred embodiment, the formulation is designed to deliver antigens to individuals in a manner designed to promote a Th1-type mediated immune response and/or in a manner designed to suppress a Th2 response. In still another embodiment, the formulation effects preferential release of the antigen within APCs. For example, various synthetic, biodegradable polymeric microsphere formulations were prepared containing **peanut** allergen. Microspheres based on poly(lactide-co-glycolide) (75:25) containing an acid end group (0.1% loaded with allergen) had the lowest amount (<20 ng) of **peanut** protein detected on the outside of the microsphere and the best range of **peanut** protein allergens contained within the microspheres (having mol. wts. ranging from 15 kDa to 70 kDa).

L16 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN
2001:416791 Document No. 135:32734 Passive desensitization. **Caplan, Michael** (Panacea Pharmaceuticals, LLC, USA). PCT Int. Appl. WO 2001039799 A2 20010607, 76 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US33125 20001206. PRIORITY: US 1999-455294 19991206;

US 2000-PV213765 20000623; US 2000-PV235797 20000927.

AB IgE-blocking agents and methods of their use have been developed for desensitizing an individual to an antigen. These IgE-blocking agents work by blocking the antigen-binding site of the IgE mols. and thereby preventing the antigen from binding. These agents typically have up to one IgE binding site present per mol. so as to prevent any crosslinking of IgE which could lead to an allergic reaction. Methods of using these novel IgE blocking agents include administering the agents to alleviate or prevent allergic reactions as well as administering the agents to decrease the risk of allergic reactions during immunotherapy or "rush" immunotherapy. Compns. and kits comprising these IgE binding agents are also provided.

L16 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2005 ACS on STN

2000:666624 Document No. 133:251267 Immunostimulatory nucleic acids and antigens. Sosin, Howard B.; **Caplan, Michael J.** (Panacea Pharmaceuticals, Llc, USA). PCT Int. Appl. WO 2000054803 A2 20000921, 103 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US7213 20000316. PRIORITY: US 1999-PV124595 19990316; US 1999-PV125071 19990317.

AB The present invention provides methods and compns. for modulating an individual's immune response to antigens. It is an aspect of the present invention that allergic responses to antigens, which in some cases lead to asthma and even anaphylaxis, can be treated or prevented by administering compns. having immunostimulatory oligonucleotides having unmethylated CpG sequences. It is another aspect of the present invention that allergies to antigens, especially one that result in asthma and anaphylaxis, can be treated or prevented by administering compns. containing immunostimulatory oligonucleotides having unmethylated CpG dinucleotide sequences and further comprising antigen(s), fragments of the antigen, mixts. of fragments of the antigen, antigens modified to reduce Th2-type immune responses, and fragments of the antigen modified to reduce Th2-type immune responses. Cellular systems for studying immunostimulation by CpG containing nucleic acids include in vivo, in vitro or ex vivo systems.

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	108.27	108.48
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.95	-10.95

STN INTERNATIONAL LOGOFF AT 15:56:27 ON 02 SEP 2005